REMARKS

No amendments are made to the claims herein. Hence no issues of new matter are presented.

I. Response to Double Patenting Rejection

Claims 1-3 and 5-30 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-30 of copending Application No. 10/201,303. It is the Examiner's position that the claims of the present application fall within the scope of the claims of the '303 application and would therefore be covered by any patent granted on the '303 application.

Since the rejection is provisional, Applicants defer taking any specific action until the claims in either one of the present application or the '303 application are indicated as allowable.

II. Response to Claim Rejections Under 35 U.S.C. § 103

A. Craig et al in view of Osada et al

1. Claims 1, 5-10 and 13-27 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over EP 496308 to Craig et al in view of JP 63-303931 to Osada et al.

According to the Examiner, Craig et al teaches a pharmaceutical composition in a form adapted for intranasal administration which comprises a generally aqueous suspension prepared by water alone or water and a physiologically acceptable non-aqueous vehicle, such as polyethylene glycol, and which may additionally contain preservatives; surfactants; isotonicity-adjusting agents; viscosity enhancers such as carboxymethylcellulose sodium, gelatin, guar gum, hydroxypropylmethyl cellulose, or methylcellulose, and preferably microcrystalline cellulose with sodium carboxymethylcellulose; and other additives.

The Examiner recognizes that Craig et al does not disclose the osmolarity of the disclosed compositions. The Examiner relies on Osada et al for the teaching that an intranasal drug formulation improves absorptivity of an active substance through the nasal mucosa into blood, exhibiting effective activity to release the active agent at a low rate of administration without an accompanying harmful reaction. According to the Examiner, Osada et al also teaches that their formulation exhibits low toxicity and stimulation and is resistant to the decomposition of the active component. These improvements are said to be achieved by suppressing the osmotic pressure ratio of an aqueous solution of the active substance to below a specific level, particularly less than 1, preferably between 0.3 and 0.1. The Examiner further states that a ratio of 1 is equivalent to an osmotic pressure of 290 mOsm and therefore Osada et al clearly suggests an osmolarity within the claimed range.

It is the Examiner's position that one of ordinary skill in the art would have been motivated to combine the teachings of Craig et al and Osada et al and rely on the teachings of these references to prepare intranasal formulations and decrease the osmolarity in order to improve absorption. Further the Examiner asserts that one of ordinary skill in the art would have expected to achieve an intranasal composition with increased absorption and decreased toxicity.

Applicants respectfully traverse the rejection and submit that the disclosure of Craig et al is similar to the disclosure of Kim et al. Thus, the evidence already of record, specifically the Declaration under 37 C.F.R. § 1.132 filed on August 13, 2001, which establishes that the disclosed compositions of Kim et al do not have an osmolarity less than 290 mOsm, is sufficient to establish that the disclosed compounds of Craig et al (which are similar to those taught by

Kim et al) do not have an osmolarity within the presently claimed range of 72 mOsm or less. Further, the Declaration under 37 C.F.R. § 1.132 is sufficient to establish unexpectedly superior results of the claimed invention over the compounds disclosed in Craig et al based upon the similarity of those compounds with the compounds disclosed by Kim et al for the same reasons that the present invention provides unexpectedly superior results over Kim et al already of record.

With respect to Osada et al, Applicants submit that Osada et al (referred to as Nagata et al) is discussed in the present specification on page 2, lines 29-37. It is disclosed in the present specification that the composition disclosed by Osada et al and other prior art compositions are not adequately transported or do not adequately permeate the mucosa tissue and that the addition of absorption enhancers causes irritation. See page 3, lines 14-31. Even further, it is discussed in the present specification on page 4, lines 37 to page 5, line 17 that one would not have reasonably expected to achieve the present invention, which permits enhanced absorption regardless of the type of drug in view of conflicting prior art teachings. In this regard it is noted that Osada et al teaches increased bioavailability of growth hormone releasing factor at an osmotic pressure ratio of 290 mOsm or less and Ohwaki and Awazu teach increased bioavailability of the drug at an osmolarity above 290 mOsm and an osmolarity of 285 mOsm when compared to an osmolarity of 174 mOsm, respectively. Applicants also note that in the Declaration of Atsuhiro Nagano filed on August 13, 2001, it is stated that it is an established rule that an osmolarity of a pharmaceutical composition for application to the mucosa should be adjusted a little higher than the mucosal osmolarity of 290 mOsm.

In view of the above, one of ordinary skill in the art would not have been motivated to combine the references as suggested by the Examiner. Further, the prior art generally teaches increasing the osmolarity to achieve increased absorption based upon the disclosures of Ohwaki and Awazu. Thus, one of ordinary skill in the would not have had a reasonable expectation of success in achieving the claimed invention of a pharmaceutical composition for application to the mucosa, which permits enhanced absorption regardless of the type of drug used, and having an osmolarity of 72 mOsm or less based upon the general teachings of the art to prepare mucosal preparations having an osmolarity a little bit higher than 290 mOsm.

In addition, the claimed invention has a 10 to 20-fold increase in bioavailability due to osmotic pressure when compared to an isotonic solution as compared to a 3-fold increase when compared to an isotonic solution for a composition as disclosed in Osada et al as discussed in the present specification. Thus, the present invention provides unexpectedly superior results when compared to the closest prior art example.

Accordingly, Applicants respectfully request withdrawal of the rejection.

2. Claims 2, 3, 28, 29 and 30 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Craig et al in view of Osada et al.

The Examiner states that the combination of references does not teach the inclusion of a hemostatic agent. It is the Examiner's position that it would have been obvious to one of ordinary skill in the art to include a hemostatic agent in an intranasal mucosal formulation to prevent any unwanted bleeding from the surface of the mucosal tissue. The Examiner further indicates that it appears as if the use of a hemostatic agent is no more than the addition of a

known material based on its suitability for its intended use, which is obvious absent a showing of criticality and unexpected results attributed to the specific ingredient selected.

Applicants respectfully traverse the rejection and submit that the rejected claims are distinguished over Craig et al in view of Osada et al for the reasons set forth above by virtue of their dependency on claim 1. Accordingly, Applicants respectfully request withdrawal of the rejection.

B. Craig et al in view of Osada et al and further in view of Yamamoto et al

Claims 11 and 12 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Craig et al in view of Osada et al and further in view of US '580 to Yamamoto et al.

The Examiner states that the combination of Craig et al and Osada et al do not teach the use of glucose as an osmotic controlling agent. The Examiner relies on Yamamoto et al for the teaching that both sodium chloride and glucose are known to help in controlling the osmotic pressure of a liquid composition. It is the Examiner's position that one of ordinary skill in the art wold have been motivated to use any well known osmotic controlling agent such as sodium chloride or glucose when attempting to alter the osmotic pressure of a particular formulation.

Applicants respectfully traverse the rejection and submit that the rejected claims are distinguished over Craig et al and Osada et al for the reasons set forth above by virtue of their dependency on claim 1. Yamamoto et al does not cure the deficiencies of the combination of Craig et al and Osada et al. Thus, the present invention is not rendered obvious over the prior art references, whether taken alone or in combination.

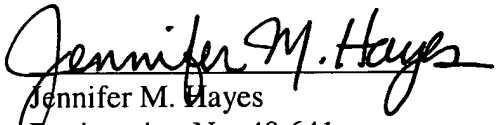
Accordingly, Applicants respectfully request withdrawal of the rejection.

III. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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